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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,532	05/25/2001	Beverly L. Davidson	9431-16065	4232

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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,532	DAVIDSON ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/30/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed June 30, 2005 (herein after referred to as "the response") has been entered. Claims 19 and 21 have been amended. Claims 1-3, 5-7, and 11-14 have been cancelled.

The Declaration of Dr. Davidson, filed June 30, 2005, is considered herein.

Claims 19-21 remain pending.

The rejection of Claims 1, 2, 5, and 6 under 35 U.S.C. 102(a) as being anticipated by Bosch et al. (2000) is withdrawn in view of the cancellation of these claims.

The rejection of Claims 19 and 21 under 35 U.S.C. 102(a) as being anticipated by Bosch et al. (2000) is withdrawn in view of the amendments to the claims, which now recite an FIV vector instead of a lentiviral vector.

The rejection of Claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by Mochizuki et al. (1998) is withdrawn in view of the cancellation of these claims.

The rejection of Claims 1-3, 5-7, and 11-14 under 35 U.S.C. 103(a) as being unpatentable over Poeschla et al. (1998), Dow et al. (1990), and Cummings et al. (1998) is withdrawn in view of the cancellation of these claims.

The rejection of Claims 1-3, 5-7, and 11-14 under 35 U.S.C. 103(a) as being unpatentable over Curran et al. (2000), Dow et al. (1990), and Cummings et al. (1998) is withdrawn in view of the cancellation of these claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 19-21 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for reasons of record advanced in the Office Actions mailed 4/1/03, 1/12/04, 7/7/04, and 6/30/05. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method of treating or preventing cerebellar neuronal degeneration, and a method of treating or preventing a central nervous system disorder. The claims are exclusively directed to *in vivo* methods that require administration of an FIV vector particle to a vertebrate subject. These claims do not encompass *in vitro* applications.

The specificaton contemplates using the claimed method *in vivo* for gene therapy applications. The specification contemplates using the claimed invention therapeutically to treat a wide variety of CNS disorders as set forth at page 6, line 21 through page 7, line 17. Thus, the only utility asserted for *in vivo* applications of the claimed methods is to produce a therapeutic effect, but the specification fails to adequately teach how to use the claimed methods therapeutically. The claims cover the use of an FIV vector encoding any protein of interest. It is well-established that the specification must teach how to use the claimed method over the full scope. With regard to *in vivo* applications, enablement is evaluated for the sole asserted utility. The only *in vivo* use asserted is for gene therapy.

For reasons of record, the specification fails to provide an enabling disclosure for therapeutic protocols.

The Declaration of Dr. Davidson, filed June 30, 2005, has been fully considered but is not found persuasive.

At paragraphs 3 and 4 of the Declaration, the Declarant refers to Alisky et al. (2000), Stein and Davidson (2002), Haskell et al. (2003), and Brooks et al. (2002). These references and the arguments relating thereto have already been addressed at pages 4-6 of the Office Action mailed 2/25/05.

At paragraph 5 of the Declaration, the Declarant describes experiments carried out to treat a β-glucuronidase deficiency in MPS VII mice, where the β-glucuronidase gene was delivered via an FIV vector comprising the gene. As discussed in the prior Office Action (mailed 2/25/05), such experiments are not deemed to evidence enablement of the claimed invention, which is directed to transducing **cerebellar** neurons, not cells of the striatum or cerebral cortex. Such experiments do not evidence enablement for treating central nervous system (CNS) disorders by transducing cerebellar neurons, as instantly claimed. Moreover, the instant specification does not provide specific guidance for expressing β-glucuronidase at therapeutic levels in the striatum and cerebral neurons as described in paragraph 5 of the Declaration. The limited teachings of the specification would not have led one of skill in the art to develop the protocol described in the Declaration. Rather the instant method is directed to providing therapeutic expression within **cerebellar** neurons. There is no support in the specification for the protocol described in the Declaration and therefore no scope of enablement will be indicated. Furthermore, the claims do not encompass the protocol described in the Declaration, because the claims require vector administration to **cerebellar** neurons, not striatal or cerebral neurons.

At paragraphs 6 and 7 of the Declaration, the Declarant concludes that based on the results obtained with an FIV vector encoding β-glucuronidase and a vector encoding TPP-I (Haskell et al., 2003), she would expect that lentivirus-mediated gene delivery of therapeutic proteins would also be successful in providing expression in cerebellar neurons with a therapeutic effect. However, the claims cover the treatment and prevention of any central nervous system disorder using an FIV vector encoding any protein of interest. Given that the gene therapy art is highly unpredictable, for reasons of record, the very broad scope of the claims, and further given that the examples referred to in the Declaration fall outside

the scope of the claims, the Examiner does not find that the Declaration supports enablement of the claimed invention.

At page 5, paragraph 2 of the response, Applicants assert that the Rubanyi et al. (2001) reference cited by the Examiner actually evidences the feasibility of gene therapy techniques because there were 368 gene therapy clinical protocols or trials in progress world wide. However, this does not speak to predictability. The existence of 368 gene therapy trials does not indicate that all gene therapy protocols, including those instantly claimed, can be developed using routine experimentation. As discussed in the prior Office Actions, the prior art shows that, in the gene therapy field, intensive investigation has met with limited success. Applicants' suggestion that "**ALL** gene therapy methods (emphasis original)" must fail in order to "provide a proper basis for a rejection under 35 U.S.C. § 112, first paragraph" is not found persuasive, because a *Wands* factors analysis, as set forth in the prior Office Actions, is the basis for the rejection under 35 U.S.C. 112, first paragraph, not a reliance on the failure of **ALL** gene therapy methods, as Applicants suggest.

At page 5, paragraph 2 of the response, Applicants assert that "the fact that the claims might encompass inoperative embodiments is not a proper basis for rejection" and further that "[s]o long as it is clear that some embodiments render the claims operative, the inclusion of possible inoperative species cannot invalidate the claim under 35 U.S.C. § 112, first paragraph." Applicants are reminded that **no scope of enablement has been indicated**. Thus, the issue is not whether the claims cover inoperative embodiments, but whether they cover any operative embodiments at all. For reasons of record, they do not.

At page 6 of the response, Applicants reiterate their arguments with regard to β-galactosidase expression and with regard to the Haskell et al. (2003) and Brooks et al. (2002) references. These arguments have already been addressed at length at pages 4-6 of the prior Office Action (mailed 2/25/05) and will not be reiterated here.

At page 7, paragraph 1 of the response, Applicants assert that they have shown successful delivery and expression in cerebellar neurons. Nevertheless, as explained in the prior Office Action, gene delivery is not gene therapy and the instant claims require a therapeutic effect or prevention of a disease. Applicants' arguments are not commensurate in scope with the scope of the claims. The references cited in Applicants' response and by the Examiner provide clear evidence that **intensive effort** has been applied to the development of gene therapy protocols with minimal success.

None of the references cited demonstrate that β-galactosidase gene expression is predictive of a therapeutic effect.

Thus, the rejection is maintained for reasons of record.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER